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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/735,335	12/12/2003	Doddabele L. Madhavi	BIO 2-016	3791

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EXAMINER	
MAIER, LEIGH C	
ART UNIT	**PAPER NUMBER**
1623	

MAIL DATE	DELIVERY MODE
05/31/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/735,335	MADHAVI ET AL.	
	Examiner	Art Unit	
	Leigh C. Maier	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-7,11,15-17 and 19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-7,11, 15-17 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 26, 2007 has been entered. Applicant's remarks accompanying the RCE have been fully considered and are addressed insofar as they pertain to the new grounds of rejection.

Claims 1 and 11 have been amended. Claims 2-4, 8-10, 12-14, 18 and 20 have been canceled. Claims 1, 5-7, 11, 15-17 and 19 are pending. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Any objection or rejection not expressly repeated has been withdrawn.

Claim Rejections - 35 USC § 102

Claims 1, 5-7, 11 and 15-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Mele et al (Carbohyd. Res., 2002).

Mele teaches the preparation of a complexes comprising lycopene with α–cyclodextrin or β–cyclodextrin. The complexes are isolated by freeze-drying. See 1st paragraph under section 3 at page 1134. The reference is silent regarding the molar ratio of the complex that is formed. However, given the structure of carotenoids and how cyclodextrins form complexes in general, it

would be expected that the cyclodextrin:carotenoid ratio would be about 1:1 or 2:1. Since the Office does not have the facilities for preparing the claimed materials and comparing them with prior art inventions, the burden is on Applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980).

Claims 1, 5, 11, 15 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Mele et al (Carbohyd. Res., 1998).

Mele teaches the preparation of a complex of β–carotene and γ–cyclodextrin that is isolated by freeze-drying. See 1st paragraph under section 2 at page 262. The reference is silent regarding the molar ratio of the complex that is formed. As discussed above, it would be expected that the cyclodextrin:carotenoid ratio would be about 1:1 or 2:1, and the burden is on Applicant to show a novel or unobvious difference between the claimed product and the product of the prior art.

Claims 1, 6 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Pfitzner et al (BBA, 2000).

Pfitzner teaches the preparation of MβCD complexes with β–carotene, lycopene, lutein and zeaxanthin. See section 2.2. The products are not isolated by freeze-drying. "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious

from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted) As above, the burden is on Applicant to demonstrate a novel or nonobvious difference.

Claims 1 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Szente et al (J. Incl. Phenom., 1998).

Sjente teaches the preparation of complexes comprising β–carotene and various cyclodextrins. See Table V. The products are prepared using suspension and coprecipitation techniques. The reference is silent regarding the actual method of isolation. As above, patentability is determined by the product itself, and the burden is on Applicant to demonstrate a novel or nonobvious difference.

Claim Rejections - 35 USC § 103

Claims 1, 5-7, 11 and 15-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mele et al (Carbohyd. Res., 2002).

Mele teaches as set forth above. The reference discusses the desirability of increasing the bioavailability of carotenoids, including lycopene, β–carotene, lutein and zeaxanthin, for their use in products such as drugs and cosmetics. One method for doing this is the encapsulation of the carotenoid in a cyclodextrin. See section 1. The reference does not exemplify complexes of all the carotenoids with a cyclodextrin.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare cyclodextrin (α or β) complexes with any of the carotenoids discussed by Mele in order to improve their bioavalability as taught in the reference. One of ordinary skill would be motivated to isolate them by freeze-drying because that is the method taught in the reference. In the absence of unexpected results, one of ordinary skill would reasonably expect success in preparing these compounds by this method because it is expressly suggested in the art.

Claims 1, 5-7, 11 and 15-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mele et al (Carbohyd. Res., 2002) in view of either of (1) Mele et al (Carbohyd. Res., 1998) or (2) Szente et al (J. Incl. Phenom., 1998).

Mele '02 teaches as set forth above. The reference does not teach the full range of recited cyclodextrins.

Mele '98 and Szente teach as set forth above.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare complexes comprising any of the carotenoids discussed by Mele '02 with any cyclodextrin known to complex with a carotenoid, such as those taught by Mele '98 or Szente. One of ordinary skill in the art would be motivated to prepare these complexes in order to increase their bioavailability as taught by Mele '02. The artisan would reasonably expect success in isolating them by freeze drying because this method is also taught by this reference.

Applicant has submitted data purporting to be evidence of unexpected results. Any such evidence would not overcome rejections to subject matter specifically rejected as being

anticipated, discussed above. Although it is the opinion of the examiner that the full scope embraced by the claims is anticipated or obvious, it is noted that every possible carotenoid/cyclodextrin combination is not anticipated, and there may be unexpected results with one or more of these combinations.

The data submitted by Applicant compares the bioavailability spray-dried lutein/γ-CD with freeze-dried lutein/γ-CD and demonstrates that freeze-dried complex has greater bioavailability in an *in vitro* assay. The examiner is not persuaded that this comparison is conclusive in the context of the invention. The *in vitro* assay demonstrates that the freeze-dried product has greater uptake by the Caco-2 cells. However, intestinal absorption is only one factor determining bioavailability. Another factor is degradation or metabolism that occurs before absorption. Applicant admits "the carotenoids are not completely protected from degradation by the complexation, [so] further formulations are necessary for incorporation into the soft gelatin capsules" and further discusses the need for other excipients. See page 7, lines 22-30. It may be that without other excipient(s) the carotenoid is so degraded before it gets to the point of being absorbed, that the added uptake by the freeze-dried product is negligible. Furthermore, it may be that one would see a different result in the in vitro assay if another protective excipient, such as oil, were present. This cannot be determined by the data submitted.

Double Patenting

Claims 1 and 5-7 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over new claims 39-46 of copending Application No. 10/309,999. The claims of '999 are drawn to a coated carotenoid/cyclodextrin complex that

is coated with a coating agent. The claims do not require freeze-drying in the preparation of the complex or recite a molar ratio. However, the written description of the product specifically suggests freeze-drying (see paragraph [0020]). Furthermore, as discussed above, the molar ratio of the complexes would be determined by the structure of the carotenoid and the particular cyclodextrin. It would be within the scope of the artisan to select any appropriate drying method.

Applicant's arguments filed February 26, 2007 have been fully considered but they are not persuasive.

Applicant argues that "the '999 application only enables spray drying." (Original emphasis.) Perhaps Applicant intends that the applicant only *exemplifies* spray drying because freeze drying is a well-known technique requiring little in the way of enablement other than suggesting its use. The examiner maintains that it would be obvious to one of ordinary skill to select any of the drying methods. Applicant notes the difference between the spray-dried products and the freeze-dried ones. However, the '999 products do not require spray-drying. Furthermore, if Applicant is relying on the difference in bioavailability, this has been discussed above with intestinal absorption being only one factor determining bioavailability.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Examiner's hours, phone & fax numbers

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh Maier whose telephone number is (571) 272-0656. The examiner can normally be reached on Monday, Wednesday and Thursday 7:00 to 3:30 (ET).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Anna Jiang (571) 272-0627, may be contacted. The fax number for Group 1600, Art Unit 1623 is (571) 273-8300.

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Leigh C. Maier

Leigh C. Maier
Primary Examiner
May 29, 2007